

ENBREL® UTILIZATION MANAGEMENT CRITERIA

DRUG CLASS: Disease Modifying Anti-Rheumatic Drug (DMARD)

BRAND NAME: Enbrel®

GENERIC NAME: Etanercept

Enbrel® is supplied as 25-mg lyophilized powder (vial) for subcutaneous injection; (GCN = 052651)

FDA INDICATIONS:

Etanercept is a tumor necrosis factor (TNF)-receptor fusion protein that blocks the interaction of TNF with receptors. It is approved for the following indications:

- Reduction of sign and symptoms, inhibition of structural damage progression, and improvement of physical function in patients with moderately to severely active Rheumatoid Arthritis (RA). Etanercept can be used in combination with methotrexate in patients who do not respond adequately to methotrexate alone.
- Reduction of signs and symptoms of moderately to severely active polyarticular-course juvenile rheumatoid arthritis in patients who have had an inadequate response to one or more DMARDs.
- Reduction of signs and symptoms and inhibition of structural damage progression of active arthritis in patients with Psoriatic Arthritis. Etanercept can be used in combination with methotrexate in patients who do not respond adequately to methotrexate alone.
- Reduction of the signs and symptoms in patients with Ankylosing Spondylitis.
- Chronic moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

ICD-9 CODES:	Rheumatoid Arthritis	714.0
	Juvenile Rheumatoid Arthritis	714.3
	Psoriatic Arthropathy	696.0
	Ankylosing Spondylitis	720
	Plaque Psoriasis	696.1

BENEFIT DESIGN:

Rheumatoid and Psoriatic Arthritis: Coverage is provided immediately (without initiating a coverage review) for the treatment of rheumatoid and psoriatic arthritis in the presence of a prescription within the previous 18 months for any of the following disease-modifying anti-rheumatic drugs (DMARDs):

- Methotrexate
- Leflunomide (Arava®)
- Etanercept (Enbrel®)
- Adalimumab (Humira®)
- Anakinra (Kineret™)

In situations where none of the above DMARDs exist in history, coverage for Enbrel® is determined through the coverage authorization criteria.

Plaque Psoriasis (chronic moderate to severe): Coverage is provided immediately (without initiating a coverage review) for the treatment of plaque psoriasis in the presence of a prescription within the previous 18 months for any of the following drugs and if the prescribing physician is a dermatologist:

- Methoxsalen (Oxsoralen®)
- Methotrexate
- Cyclosporine
- Acitretin (Soriatane®)
- Etanercept (Enbrel®)
- Efalizumab (Raptiva®)

In situations where the above does not apply, coverage for Enbrel® is determined through the coverage authorization criteria.

An independent licensee of the Blue Cross and Blue Shield Association. ©,SM Marks of the Blue Cross and Blue Shield Association. SM1 Mark of Blue Cross and Blue Shield of North Carolina. V471, 4/08

Your plan for better health.™ | bcbsnc.com



**BlueCross BlueShield
of North Carolina**

COVERAGE AUTHORIZATION CRITERIA:

Coverage is provided if one of the following bullets applies:

- **Rheumatoid or Psoriatic Arthritis** when a patient has experienced a therapeutic failure/inadequate response with methotrexate

OR

Is unable to receive methotrexate (e.g. use of methotrexate is contraindicated in the patient)

OR

Rheumatoid or Psoriatic Arthritis is rapidly progressive and advancing

- Diagnosis of **Ankylosing Spondylitis**
- **Plaque Psoriasis, Pustular Psoriasis, or Erythrodermic Psoriasis**

AND

Member is being managed by a dermatologist

AND

Body Surface Area (BSA) involvement of at least 5%

OR

Involvement of the palms, soles, head and neck, or genitalia, causing disruption in normal daily activities and/or employment

AND

Failure of systemic therapy (methotrexate, cyclosporine, Soriatane,) or patient has contraindication to these treatments

*Coverage of Enbrel® is not provided for use in combination with Kineret™, Remicade®, Humira®, Raptiva®, or Amevive®.

For all covered indications, the provider must have considered and screened for the presence of latent tuberculosis (TB) infection.

BLACK BOX WARNINGS:

None

RATIONALE:

- For RA and Psoriatic Arthritis, a treatment program that includes methotrexate as initial therapy may be considered for most patients unless a patient has a contraindication to or is unable to receive methotrexate (e.g., such as in the presence of liver or lung disease).
- Conventional therapy for moderate to severe psoriasis includes phototherapy and/or oral medications such as methotrexate and cyclosporine. Due to the potential for serious side effects, the cost impact, and the monitoring requirements, Enbrel® is considered second-line therapy after topical treatment, phototherapy, and other systemic medications currently used for psoriasis (i.e. methotrexate, cyclosporine, Soriatane®).

DOSAGE AND ADMINISTRATION:

- **Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis:** 25mg given twice daily as a subcutaneous injection 72-96 hours apart. Doses higher than 25 mg twice weekly are not recommended.
- **Plaque Psoriasis:** 50mg given twice weekly as a subcutaneous injection 72-96 hours apart for 3 months followed by a reduction to a maintenance dose of 50mg per week.

Subcutaneous injections can be given in the thigh, abdomen, or upper arm and injection sites should be rotated. Etanercept is reconstituted with Sterile Bacteriostatic Water for Injection and should be used as soon as possible after reconstitution. If necessary, etanercept can be stored in the refrigerator for up to 6 hours after reconstitution. It can be given in combination with methotrexate, glucocorticoids, salicylates, NSAIDs, or analgesics. Etanercept can be self-administered by patients with injection technique training, but the first injection should be given under the supervision of a health-care professional.

RISK FACTORS/CONTRAINDICATIONS:

Etanercept is contraindicated in patients with sepsis or hypersensitivity to etanercept or any product component.

Serious infections and sepsis, including fatalities, have been reported with the use of etanercept in post-marketing studies. Many of these infections occurred in patients on concomitant immunosuppressive therapy that, in addition to their underlying disease, could predispose them to infections. Rare cases of tuberculosis (TB) have been observed in patients treated with TNF-antagonists, including etanercept. Patients who develop a new infection while undergoing treatment with etanercept should be monitored closely. The drug should be discontinued if a patient develops a serious infection or sepsis.

RISK FACTORS/CONTRAINDICATIONS (continued):

Treatment with etanercept should not be initiated in patients with active infections including chronic or localized infections. Physicians should exercise caution when considering the use of etanercept in patients with a history of recurring infections or with underlying conditions that may predispose patients to infections, such as advanced or poorly controlled diabetes.

Treatment with etanercept and other agents that inhibit TNF have been associated with rare cases of new onset or exacerbation of central nervous system demyelinating disorders, some presenting with mental status changes and some associated with permanent disability. The causal relationship with etanercept remains unclear. Prescribers should exercise caution in considering the use of etanercept in patients with pre-existing or recent-onset central nervous system demyelinating disorders.

Rare reports of pancytopenia including aplastic anemia, some with a fatal outcome, have been reported in patients treated with etanercept. The causal relationship to etanercept therapy remains unclear. Caution should be used in patients being treated with etanercept who have a previous history of significant hematologic abnormalities.

Two large clinical trials evaluating the use of etanercept in the treatment of congestive failure did not demonstrate efficacy. However, there was a suggestion of worse heart failure outcomes with etanercept treatment in one of the trials. There have been post-marketing reports of worsening heart failure in patients taking etanercept. Physicians should use caution when using etanercept in patients who have heart failure.

DRUG INTERACTIONS:

- Formal drug interaction studies have not been conducted with etanercept. In clinical trials, it has been given in combination with NSAIDs, corticosteroids, analgesics (acetaminophen, codeine, oxycodone, and propoxyphene), and methotrexate.
- Since TNF modulates the cellular immune response and plays a role in the host response against infection, etanercept could affect the immune response to vaccination. To date, the effects of etanercept on vaccination have not been evaluated. The manufacturer recommends against the administration of live vaccines to patients receiving etanercept.

REFERENCES:

1. Kremer JM. Rational Use of New and Existing Disease-Modifying Agents in Rheumatoid Arthritis. *Annals of Internal Medicine*. 2001; 134(8): 695-706.
2. Mease PJ, Goffe BS, Metz J, et al. Etanercept in the Treatment of Psoriatic arthritis and psoriasis: a randomized trial. *Lancet*. 2000; 356: 385-90.
3. Enbrel (etanercept). Product Information. Immunex. 2004.
4. Callen JP, Krueger GG, Lebwohl M, et. al. AAD Statement on Psoriasis Therapies. *J Am Acad Dermatol*. 2003 Nov; 49(5): 897-9.
5. National Psoriasis Foundation website. Psoriasis treatment. http://www.psoriasis.org/medical/advocacy/2003_systemicdiagram.php
6. Rangioletti F, Borenstein M, Krisner R, Kerdel F. Erythrodermic recalcitrant psoriasis: clinical resolution of infliximab. *J Dermatol Treat*. 2003 Dec; 14(4): 222-5.
7. Barland C, Kerdel FA. Addition of low-dose methotrexate to infliximab in the treatment of a patient with severe, recalcitrant pustular psoriasis. *Arch Dermatol*. 2003 Jul; 139(7): 949-50.